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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/328,975	06/09/1999	JOHN A. WOLFF	MIRUS009	7574

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MARK K JOHNSON
P O BOX 510644
NEW BERLIN, WI 531310644

EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1635	

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16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/328,975	Wolff
Examiner	**Art Unit**
Richard Schnizer	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 19, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3-8, 10, and 12-19* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3-8, 10, and 12-19* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jun 9, 1999* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/19/03 has been entered.

An amendment was received and entered as Paper No. 15 on 2/19/03. Claim 2 was canceled as requested. Claims 1, 3-8, 10, and 12-19 are pending and under consideration in this Office Action.

Rejections Withdrawn

The rejection of claim 13 under 35 U.S.C. 112, first paragraph for new matter is withdrawn in view of Applicant's arguments, but is replaced by the following new matter rejection necessitated by Applicant's amendment.

The rejection of claim 3 under 35 USC 112, first paragraph for lack of enablement is withdrawn in view of Applicant's amendment. It is noted however, that Applicant asserts at page 3 of the response that claim 3 has been amended to recite "polyion" in place of "polycation", but no such amendment was received by the Office.

The rejection of claim 17 under 35 USC 112, first paragraph for lack of enablement is withdrawn in view of Applicant's argument.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 8-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8-14 haves been amended to require a polyanion polymer having a molecular weight of at least 30 kDa. The specification contains no literal support for this amendment, so it constitutes new matter. Applicant points for support to Example 1, beginning on page 22, line 25. This example discloses a the polyanionic polymers polyglutamic acid (49 kDa), polyaspartic acid (36 kDa), succinylated PLL (no molecular weight given), and pCILuc (no molecular weight given). Nowhere in this section is there any support for the genus of all polyanion polymers having a molecular weight of at least 30 kDa. Thus the amendment constitutes new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-18 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record in Paper No. 12..

Claims 15-18 are indefinite for the following reasons. These claims, in 'b)' require the following: "attaching a charged polymer to the complex in sufficient amount to change the complex net charge wherein the complex has a net charge more negative than the complex in the previous step". This passage is unclear because the method steps cannot result in the recited process. The complex in 'a)' has a given net charge. Attaching a charged polymer to that complex does not change the net charge of the complex, it results in a new complex that has a net charge different than the previous complex. It is suggested that 'b)' should be amended to read "attaching a charged polymer to the complex of 'a)' in sufficient amount to form a new complex having a net charge more negative than the complex in 'a)'". Another way to understand the indefiniteness is to consider the antecedent basis for the third instance of the phrase "the complex" in 'b)'. The only antecedent for this "complex" is the "complex" recited in 'a)', yet the claim requires that this "complex" cannot be the "complex from 'a)' which is referred to as "the complex in the prior step".

Claims 15-18 are indefinite because they recite in step b) "the prior step" without antecedent basis. The claim provides no limitation on the number of steps that may occur between ' a)' and 'b)', so it is unclear to which "step" the claim refers..

Claim 17 is indefinite because it recites a non sequitur. Specifically, it requires first that "the polymer" is selected from the group **consisting** of PLL and PEI, but then allows the polymer to comprise a variety of compounds that are not PLL or PEI, including succinylated PLL, succinylated PEI, polyglutamic acid, polyaspartic acid, DNA, RNA, and negatively charged proteins, etc. Because these compounds are not within the scope of the group of compounds consisting of PLL and PEI, the claim is indefinite.

Response to Arguments

Applicant's arguments filed 2/19/03 have been fully considered but they are not persuasive.

Applicant's arguments at paragraph 2 of page 4 of the response are unpersuasive because they are based on errors of fact. For example, Applicant states that "claim 16 actually states that "the polycation" be selected from PLL and PEI." This is incorrect, claim 16 does not recite the word "polycation". Applicant states that "claim 17 requires a "negatively charged polyion" and does not use the term 'polymer'." This is incorrect. Claim 17 recites "The complex of claim 16 wherein the polymer", etc. Nowhere does claim 17 recite "negatively charged polyion", as asserted by Applicant. As such, the basis for Applicant's arguments is nonexistent, and the arguments are unpersuasive.

Applicant further argues at paragraph 3 of page 4 that claims 15-17 are believed to be definite because "[t]he "consisting of" language refers to the monomer-polymers individually, not the polymer which results from the attachment of two monomer-polymers." This is unpersuasive for two reasons. First, the claims do not recite the term "monomer-polymer", so Applicant's arguments are not applicable. Second, because claim 17 depends from claim 16, it can only further limit claim 16, it cannot broaden claim 16. Claim 16 clearly limits the identity of "the polymer" to the group consisting of PLL and PEI. The only antecedent for "the polymer" recited in claim 17 is "the polymer" recited in claim 16, *ergo* the polymer of claim 17 must be either PLL or PEI, and cannot comprise any of the molecules set forth in the Markush group of claim 17.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8, 10, 12, 14-16, and 18 stand rejected under 35 U.S.C. 102(b) as being anticipated by Erbacher et al (Drug Deliv. 4:173-179, 1997), as evidenced by Basu et al (Biochim.

Biophys. Acta 533 (1): 66-73, 1978), and GenBank Accession No. CAA41735, for the reasons of record in Paper No. 12.

Erbacher teaches compositions comprising polylysine/DNA complexes to which a negatively charged protein, lactosylated bovine serum albumin (BSA), was bound in a solution of neutral pH (DMEM). See abstract; page 175, first full paragraph of column 1; and Fig. 1 on page 175. It is noted that the specification at page 12, lines 24-27 defines a polyanion as a polymer that may contain positive charges but retains a net negative charge. BSA is a polyanionic polymer at neutral pH as evidenced by Basu et al (Biochim. Biophys. Acta 533 (1): 66-73, 1978), who teaches that BSA has a pI of either 4.8 or 5.6, and as evidenced by the sequence disclosed in GenBank Accession No. CAA41735. The complex is used to deliver nucleic acids to cells in vitro. See abstract.

Thus Erbacher anticipates the claims.

Claims 8, 10, 12, 14-16, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Plank et al (J. Biol. Chem 269(17): 12918-12924, as evidenced by Richards et al (J. Chromatog. (1997) 690(1-2): 43-54), and GenBank Accession No. AAB22049 (5/7/1993).

Plank teaches DNA delivery complexes comprising DNA, polylysine covalently attached to transferrin, free polylysine, and negatively charged endosomolytic peptides. See abstract; Table I on page 12920 which gives the sequences of the peptides; and Fig. 3, panel A on page 12922.

In this case the polyanion polymer having a molecular weight of at least 30 kDa is considered to be transferrin. It is noted that the specification at page 12, lines 24-27 defines a polyanion as a polymer that may contain positive charges but retains a net negative charge. Transferrin meets this limitation as evidenced by GenBank Accession No. AAB22049 which shows that transferrin is 698 amino acids long, containing numerous negatively charged residues. Estimating 115 Daltons per amino acid, transferrin has a molecular weight of 80 kDa. Richards (1997) provides evidence that transferrin is negatively charged at pH greater than 6.25 by measuring the isoelectric points of apotransferrin, and monoferric and differic transferrin. The highest pI measured was 6.25. Plank teaches that complexes were formed at pH 7.3 (see e.g. legend to Fig. 3), so the transferrin of Plank is a polyanionic polymer of greater than 30 kDa.

Plank also teaches delivery of the complexes in vitro. See abstract.

Thus Plank anticipates the claims.

Claims 8, 10, 12, 14 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by either one of Gao et al (HUMAN GENE THERAPY, (1993 Feb) 4 (1) 17-24) or Kupfer et al (HUMAN GENE THERAPY, (1994 Dec) 5 (12) 1437-43), as evidenced by Richards et al (J. Chromatog. (1997) 690(1-2): 43-54), and GenBank Accession No. AAB22049 (5/7/1993).

Gao and Kupfer each teach a method of delivering a nucleic acid to a cell in vivo comprising a forming a complex consisting of three types of polymers, a negatively charged nucleic acid, a polycation, and a negatively charged protein, transferrin, and delivering the

complex to cells in a mammal in vivo. See abstracts. In this case the polyanion polymer having a molecular weight of at least 30 kDa is considered to be transferrin. It is noted that the specification at page 12, lines 24-27 defines a polyanion as a polymer that may contain positive charges but retains a net negative charge. Transferrin meets this limitation as evidenced by GenBank Accession No. AAB22049 which shows that transferrin is 698 amino acids long, containing numerous negatively charged residues. Estimating 115 Daltons per amino acid, transferrin has a molecular weight of 80 kDa. Richards (1997) provides evidence that transferrin is negatively charged at pH greater than 6.25 by measuring the isoelectric points of apotransferrin, and monoferric and differic transferrin. The highest pI measured was 6.25. Both Gao and Kupfer teach that complexes were formed in HBS buffer (pH 7.3) (see e.g. Gao at page 18, column 1, lines 1-6 of third full paragraph, and Kupfer at sentence bridging pages 1438 and 1439), so the transferrins of Gao and Kupfer are a polyanionic polymers of greater than 30 kDa.

Thus Gao and Kupfer each anticipate the claims.

Claims 8, 10, 12, 14 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Boussiff et al (Proc. Nat. Acad. Sci. 92:7997-7301, 8/1995), as evidenced by the 1998 Promega catalog.

Boussiff teaches a method of making nucleic acid/PEI complexes, and methods of delivering the complexes in vitro and in vivo. The nucleic acid can be considered to be the polyanion of the claims, and PEI is the polycation. See abstract, and paragraph bridging columns

1 and 2 on page 7298. The nucleic acid can be a plasmid e.g. pGL2-Luc. See page 7297, column 2, line 7 of second full paragraph. The 1998 Promega catalog teaches that plasmid pGL2-Luc is 5.6 kb in length. See page 245. .Estimating 660 D per base pair, the molecular weight of pGL2-Luc is about 3.7 million D, thus meeting the claim limitation requiring that the polyanion be at least 30 kDa. With regard to claim 19, the complexes are considered to contain multiple copies of nucleic acids and polycations, in view of the fact that their sizes range from 0.1 to 1 micron and Boussiff identifies them as "multimolecular " particles. As such, the Boussiff anticipates claim 19 which requires a complex of three polymers having a net charge in solution wherein two of the polymers have a net negative charge. One of these polymers consists of the nucleic acid. The claim is anticipated because it does not limit the identity of the second anionic polymer, which can also consist of the nucleic acid. Because more than one nucleic acid is contained in each complex, each complex comprises the three polymers of the claim.

Thus Boussiff anticipates the claims.

Claims 8, 10, 12 and 14 stand rejected under 35 U.S.C. 102(e) as being anticipated by Kabanov et al (US Patent 5,656,611, issued 8/12/97), as evidenced by the 1995 New England BioLabs catalog.

Kabanov teaches a complex comprising nucleic acids complexed with a polycationic block copolymer. See column 3, lines 1-37, especially lines 1 and 34-37. The nucleic acid can be considered to act as the polyanion polymer. The nucleic acid may be pbeta-gal, which comprises

pUC19 (see e.g. column 13, lines 48-52). The 1995 New England BioLabs catalog teaches that plasmid pUC19 is 2.7 kb in length. See page 186. Estimating 660 D per base pair, the molecular weight of pUC19 is about 1.8 million D, thus meeting the claim limitation requiring that the polyanion be at least 30 kDa. Thus Kabanov anticipates the claims.

Claims 8, 10, 12, and 14 stand rejected under 35 U.S.C. 102(b) as being anticipated by Baker et al (Nucl. Acids Res. 25(10): 1950-1956, 5/1997), for the reasons of record in Paper No. 12.

Baker teaches compositions comprising 170 kb bacterial artificial chromosomes complexed with either polylysine/adenovirus conjugates or polyethyleneimine/adenovirus. The nucleic acid can be considered to act as the polyanion polymer recited by claims 8 and 10. The molecular weight of a 170 kb nucleic acid is approximately 112,000,000 D. Polylysine and polyethyleneimine are the polycations.

Thus Baker anticipates the claims.

Claims 8, 10, 12, and 14 stand rejected under 35 U.S.C. 102(b) as being anticipated by Katayose et al (Bioconj. Chem. 8:702-707, 1997), as evidenced by Christens-Barry et al (Biopolymers (1989) 28(9): 1515-1526).

Katayose teaches a complex comprising a linearized Col E1 plasmid, polylysine, and polyaspartic acid. See abstract, and Fig. 5, panel B which discloses an intermediate in an

exchange reaction, wherein the intermediate comprises DNA, PLL, and polyaspartic acid. Christens-Barry teaches that Col E1 is 6646 bases in length. Assuming 660 D/base pair, Col E1 has a molecular weight of about 4.4 million D, thus meeting the claim limitation requiring that the polyanion be at least 30 kDa.

Thus Katayose anticipates the claims.

Claims 8, 10, 12, 14, and 16-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Wolff et al (US Patent 6,339,067, filed 12/30/97).

Wolff teaches complexes comprising plasmid DNA and polycations. The complexes may also comprise a second polyanion. See e.g. column 21, lines 48-56, and column 28, lines 1-61. Disclosed polycations include histones, protamines, polylysine, polyarginine, polyornithine, DEAE dextran, polybrene, and polyethylenimine. See e.g. column 1, lines 21-26. Disclosed polyanions include dextran sulfate (molecular weight = 500 kDa), and the specification teaches that other polyanions could be used. See column 28, lines 37-40, and column 29, lines 1-3.

In addition to the ternary complexes described in the preceding paragraph, the claims are also anticipated by the disclosed binary plasmid DNA/PLL complexes alone. Assuming a molecular weight of 660 D/base pair, a 46 base pair long double stranded DNA has a molecular weight of greater than 30 kDa, as required by the claims. All plasmids disclosed in Wolff are double stranded and of greater length than 46 base pairs. So, the disclosed complexes of polycations and plasmid DNAs are sufficient to anticipate the claims.

Response to Arguments

Applicant's arguments filed 2/19/03 have been fully considered but they are unpersuasive.

With respect to Erbacher, Applicant argues that claim 8 recites an ionic complex, and that Erbacher does not teach an ionic complex because biotin is covalently bound to PLL. This is unpersuasive for several reasons. First, claim 8 does not recite the term "ionic", therefore it is not limited to ionic complexes and continues to embrace covalent complexes. Second, Applicant has failed to show that Erbacher does not teach an ionic complex. PLL is covalently attached to biotin, but is complexed non-covalently via a streptavidin bridge to biotinylated BSA. See Fig. 1 at page 175. Even if the claim required an ionic interaction, which it does not, Applicant has failed to show that the biotin/streptavidin interaction has no ionic character. Applicant has failed to show that the because biotin is covalently bound to PLL.

With respect to Plank, Applicant argues that the amendment overcomes the rejection because it requires a polyanion polymer of greater than 30 kDa complexed with the polycation. This is unpersuasive because Plank teaches transferrin complexed with PLL. Note that the claim does not exclude covalent complexes.

With regard to Gao and Kupfer, Applicant argues that the references do not anticipate the claims because they teach covalent rather than ionic complexes. This is unpersuasive because the claims do not require ionic complexes.

With regard to Boussiff and Kabanov, Applicant argues that a ternary complex is claimed, and that these references teach only binary complexes. This argument is unpersuasive because the

claims do not recite or require a ternary complex. Although the claims embrace ternary complexes, they do not exclude binary complexes, because they do not

With regard to Baker, Applicant argues that a streptavidin-biotin linkage is not ionic in nature. This argument is unpersuasive because it lacks any support.

With regard to Katayose, Applicant argues that the complex formed is an unstable intermediate that could not be used for the intended purpose of delivering a nucleic acid to a cell. This argument is unpersuasive because it lacks support. Applicant has not provided any evidence or logical argument that the intermediate complex is so unstable that it could not be isolated and used to deliver a nucleic acid to a cell.

Applicant further argues that the Declaration of James E. Hagstrom regarding histones complexed with DNA indicates the conception of the invention by June of 1994. Applicant indicates that although the Declaration exemplifies only one species of polycation, that species is representative of the others. This is unpersuasive because the Declaration provides no evidence that Applicant contemplated any species of polycation other than histones. Note that Claims 8, 10, 12, and 14-19 allow for cationic compounds other than histones. In fact none of these claims recites histones as a polycationic polymer. In particular, claims 10 and 16 require that the polycation must be PLL or PEI. The Declaration fails to establish that Applicant was in possession, prior to the time of filing, of any claimed composition or method other than those comprising complexes between histones and nucleic acids. For these reasons, the rejections are maintained. The rejections may be overcome by limiting the identity of the polycation to

histone, but Applicant should confirm that such an amendment would not introduce new matter into the disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Gao (1993) or Kupfer (1994), in view of Plank (1994).

Gao and Kupfer each teach a method of delivering a nucleic acid to a cell *in vivo* comprising a forming a complex consisting of a nucleic acid, polylysine, and transferrin, and delivering the complex to cells in a mammal *in vivo*. See abstracts. These references do not teach the addition of a charged polymer to the DNA/polylysine/transferrin complex.

Plank teaches DNA delivery complexes comprising DNA, polylysine covalently attached to transferrin, free polylysine, and negatively charged endosomolytic peptides. See abstract; Table I on page 12920 which gives the sequences of the peptides; Fig. 3, panel A on page 12922, and paragraph bridging pages 12920 ans 12921.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the methods of Gao or Kupfer by adding the negatively charged peptides and free polylysine of Plank. One would have been motivated to do so because the polylysine improves binding of the peptides to the complex, and because the peptides allow escape from the endosomal/lysosomal pathway, thereby allowing one to avoid degradation of DNA in the lysosomes, and enhance gene expression. See first sentence of abstract, and first sentence and lines 14-16 of first full paragraph on page 12918, column 1.

Claim 6 is included in this rejection, because several of the peptides of Plank can be considered to comprise block copolymers. For example, INF3DI, INF3DI2, INF3DI3 and INF5 consist of inverted repeats of amino acid sequences, and GALA, GALA-GLF, GALA-INF1, and GALA-INF3 comprise repeats of the blocks EA and LA. See Table I on page 12920.

Thus the invention as a whole was *prima facie* obvious.

Claims 1, 3-5, 7, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolff et al (US Patent 6,339,067, filed 12/30/97).

Wolff teaches methods of recharging cationic nucleic acid delivery compositions. DNA/polycation complexes were prepared, and then polyanions were added to the complexes in order to form a new complex with a less positive net charge. See e.g. column 21, lines 48-56, and column 28, lines 1-61. Disclosed polycations include histones, protamines, polylysine, polyarginine, polyornithine, DEAE dextran, polybrene, and polyethylenimine. See e.g. column 1,

lines 21-26. Disclosed polyanions include dextran sulfate (molecular weight = 500 kDa), and the specification teaches that other polyanions could be used. See column 28, lines 37-40, and column 29, lines 1-3.

Wolff does not teach delivery of the complexes to cells in vitro or in vivo.

It would have been obvious to one of skill in the art to deliver the complexes of Wolff to cells either in vivo or in vitro. One would have been motivated to do so because Wolff teaches that the complexes are intended to be used to transfer nucleic acids to cells in vivo. See column 4, lines 66 and 67. One would have been motivated to deliver the complexes to cells in vitro in order to assess the function of the nucleic acid prior to delivering it to an organism in vivo.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 2/19/03 have been fully considered but they are unpersuasive.

Applicant argues that amendment of the claims to recite "ionically attaching" a polymer overcomes the rejection over either one of Gao or Kupfer in view of Plank. This is unpersuasive because Plank teaches incorporation of the negatively charged peptides into the DNA/polycation complexes by ionic interaction. See abstract.

Conclusion

No claim is allowed. Claim 13 is free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER